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USE OF CHITIN FOR PROMOTING WOUND HEALING

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ABSTRACT OF THE DISCLOSURE

Wound healing compositions and the process of healing wounds with such compositions are described, the compositions containing chitin, partially depolymerized chitin or a chitin derivative.

This application is a continuation-in-part of my copending application Ser. No. 619,007 filed Feb. 27, 1967.

This invention relates to methods of promoting the healing of wounds and compositions therefor comprising chitin, and/or chitin derivatives and/or partially depolymerized chitin.

Medicine has long been interested in improving the healing of wounds. Patients suffering from diabetes or undergoing extensive cortisone treatment show extremely slow rates of healing of any wounds which they receive. Thus, surgery on such patients involves additional risks not present with other patients. Moreover, rapid healing of wounds is particularly desired for patients in tropical countries where the risk of infection is high. Rapid healing is also desired in the case of soldiers who have been wounded in a battle zone and cannot easily and quickly be removed therefrom. Acceleration of wound healing is highly desirable in the case of patients who cannot readily be immobilized, such as farm animals.

In evaluating the utility of a material to promote wound healing, a reproducible test is necessary to give comparative data. Such a test method has been described by Prudden et al. in: "The Acceleration of Wound Healing With Cartilage," Surgery, Gynecology and Obstetrics, 105:283 (1957). In this method, rats are tested in pairs, each pair receiving an identical surgical incision, only the one rat of the pair receiving a measured dose of the material whose wound healing properties is to be determined. The pair is then kept in the same cage and the tensile strength of the wounds in the two rats is determined in millimeters of mercury. The difference in the tensile strengths between the treated rat and the control rat is expressed as the percentage improvement obtained. Considering biological variance it is believed that only differences of about 10% or more are significant.

There have been several recent developments reported concerning materials which promote wound healing. In this connection U.S. Pat. No. 3,232,836 describes the parenteral administration of N-acetylglucosamine as a wound healing material. Utilizing the test method of Prudden et al. referred to in the preceding paragraph, N-acetylglucosamine showed improvement in tensile strength of only about 10% whereas Prudden and his co-workers have reported significantly larger increases in wound healing by the use of cartilage preparations from various animals. Depending on the age and species of animal and the fineness of the cartilage powder, improvements ranging from 20 to 40% in wound healing tensile strength have been reported by Prudden.

Now it has been discovered that finely divided chitin, partially depolymerized chitin, and chitin derivatives possess the ability to promote the healing of wounds.

Accordingly, one aspect of the present invention relates to novel methods of promoting and assisting the healing of wounds as, for example, damaged mammalian tissue, open ulcers, etc., and to compositions therefor.

Another aspect of the invention relates to significant improvements in wound healing strength achieved by the administration of finely divided chitin, partially depolymerized chitin or chitin derivatives to a patient.

An additional aspect of the present invention is concerned with articles of manufacture such as surgical bandages, surgical sutures, etc., containing the wound healing materials of the present invention.

These and other aspects of the present invention will be apparent from the following description.

Chitin is a polysaccharide, believed to be poly (N-acetylglucosamine) which forms the cell walls of fungi and the hard shell of insects and crustaceans. As used herein, the term "chitin" embraces naturally occurring chitin, synthetic chitin, as well as poly (N-acetylglucosamine) and its epimer poly (N-acetylgalactosamine). The partially depolymerized chitin, e.g. chitotriose, chitobiose, is a substance which retains its polymeric nature but has undergone a reduction in molecular weight (i.e. chain length) as a result of (1) enzymatic action such as by a chitinase enzyme, (2) chemical treatment such as acid hydrolysis or alkaline treatment, and (3) physical treatment.

The chitin derivatives contemplated are materials such as ethers formed with pharmaceutically-acceptable radicals and esters or salts with pharmaceutically-acceptable acids. Examples of suitable derivatives include hydroxy lower alkyl chitin such as hydroxyethyl chitin, carboxy alkyl chitin such as carboxymethyl chitin, salts of carboxy lower alkyl chitin such as the zinc salt, lower alkyl chitin such as methyl chitin and ethyl chitin, chitin acetate, chitin nitrate, chitin citrate, chitin phosphate, N-acyl derivatives derived from monocarboxylic aliphatic acids such as N-formyl, N-acetyl, N-propionyl, N-caproyl, etc.

It is preferred to use natural chitin as the wound healing accelerator. The naturally occurring chitin is preferably chitin of fungal origin, both by reason of its ready availability and its high degree of effectiveness.

The degree of improvement in wound healing obtained with the chitin materials is at least equal to and in many instances greater than that derived from the cartilage materials of the prior art. The substantial improvement in rate of healing which is obtained from the use of poly (N-acetylglucosamine), i.e., chitin, as compared to monomeric N-acetylglucosamine is particularly surprising. As compared to the great variability in cartilage depending on the animal, its age and the method of collecting the cartilage, chitin, particularly chitin of fungal origin, is a relatively uniform and easily obtained material.

The compositions of the present invention are applied using the same techniques and processes developed for cartilage, and N-acetylglucosamine. Thus, it is preferred to topically apply finely divided chitin directly to the wound surface. However, tablets, capsules or pellets of chitin may be prepared from mixtures of chitin, partially depolymerized chitin or chitin derivatives with well-known pharmaceutical excipients such as starch, sugar, certain forms of clay, etc. Such tablets, capsules or pellets may be taken orally or implanted near the situs of the wound. Alternatively, a colloidal solution may be prepared from chitin, preferably in isotonic saline, or a water-soluble derivative of chitin may be dissolved preferably in isotonic saline solution, and the solution administered intramuscularly, parenterally or intravenously.

A powder or solution of chitin or of a chitin derivative may also be used to impregnate a surgical gauze or pad which is applied to the wound. Chitin may also be dis-